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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,731	05/11/2001	Apollon Papadimitriou	20619	6504

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HOFFMANN-LA ROCHE INC.
PATENT LAW DEPARTMENT
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EXAMINER

KAM, CHIH MIN

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 03/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/853,731

Applicant(s)

PAPADIMITRIOU, APOLLON

Examiner

Chih-Min Kam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 23-35,38-42,51-55,59-61,67-77 and 83-89 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 23-35,38-42,51-55,59-61,67-77 and 83-89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/17/04;1/13/05
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Status of the Claims

1. Claims 23-35, 38-42, 51-55, 59-61, 67-77 and 83-89 are pending.

Applicants' amendment filed on January 6, 2005 is acknowledged. Applicants' response has been fully considered. Claims 23, 26, 28, 29, 34, 38, 39, 51, 67, 69, 71, 73 and 75 have been amended, and claims 1-22, 36, 37, 43-50, 56-58, 62-66 and 78-82 have been cancelled. Thus, claims 23-35, 38-42, 51-55, 59-61, 67-77 and 83-89 are examined.

Objection Withdrawn

2. The previous objection of claims 1, 3, 26, 28, 51, 67, 69, 71, 73 and 75 regarding the term "multipli-charged" or "multiply charged" is withdrawn in view of applicant's amendment to the claims, applicant's cancellation of the claim, and applicant's response at page 15 of the amendment filed January 6, 2005.

Rejection Withdrawn

Claim Rejections-Obviousness Type Double Patenting

3. The previous rejection of claims 1, 19, 26, 44 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/014,363, is withdrawn in view of applicant's amendment to the claims, applicant's cancellation of the claim in the amendment filed January 6, 2005.
4. The previous rejection of claims 1-11, 13-17, 19, 36, 44, 48-50 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of copending Application No. 10/780,297 (US 2004/0147431), is withdrawn in view of applicant's cancellation of the claim in the amendment filed January 6, 2005.

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Claim Rejections - 35 USC § 112

5. The previous rejection of claims 4-5, 9-10, 14-17 and 29-35 under 35 U.S.C. 112, second paragraph, as being indefinite, is withdrawn in view of applicant's amendment to the claims, applicant's cancellation of the claim, and applicant's response at page 16 of the amendment filed January 6, 2005.

Claim Rejections - 35 USC § 102

6. The previous rejection of claims 1-4, 6-9 and 11 under 35 U.S.C. 102(b) as anticipated by Yamazaki *et al.* (EP 0909564, April 25, 1997), is withdrawn in view of applicant's cancellation of the claim, and applicant's response at page 16 of the amendment filed January 6, 2005.

Claim Rejections - 35 USC § 103

7. The previous rejection of claims 1-4, 6-9, 11 and 13 under 35 U.S.C. 103(a) as being unpatentable over Yamazaki *et al.* (EP 0909564) in view of Rosen *et al.* (WO 92/06116), is withdrawn in view of applicant's cancellation of the claim, and applicant's response at page 17 of the amendment filed January 6, 2005.

8. The previous rejection of claims 1-4, 6-9, 11 and 13-17 under 35 U.S.C. 103(a) as being unpatentable over Yamazaki *et al.* (EP 0909564) in view of Rosen *et al.* (WO 92/06116) and Elliot *et al.* (EP 0640619), is withdrawn in view of applicant's cancellation of the claim, and applicant's response at page 17 of the amendment filed January 6, 2005.

Claim Objections

9. Claims 26-35, 38-42, 51-55, 59-61 and 77 are objected to because the claim number "26" in claim 26 was struck through.

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 67-71, 73, 75, 83, 85 and 86 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U. S. Patent 6,583,272. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 67-71, 73, 75, 83, 85 and 86 in the instant application disclose a liquid pharmaceutical composition comprising a pegylated EPO having the formula $P-(NHCO-(CH_2)_x-(OCH_2CH_2)_m-OR)_n$, wherein n is 1-3, and the pegylated EPO has the in vivo biological activity. This is an obvious variation in view of claims 1-13 in the patent which disclose a conjugate comprising an EPO glycoprotein having N-terminal α -amino group and one poly(ethyleneglycol), where EPO is linked to $-CO-(CH_2)_x-(OCH_2CH_2)_m-OR$; and the specification of the patent discloses the peg-EPO can be prepared in various formulations containing a multiple charged inorganic anion and a buffer at pH 5.5-7.0, e.g., formulation having 10 mM phosphate, 40 mM sulfate, 4% mannitol, pH 6.2 (Examples 6 and 8; Table 3; Fig. 4). In view of the teachings in the specification of the patent, it is obvious that the claims of the patent and the claims of instant application are directed to a pharmaceutical composition

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comprising a peg-EPO conjugate. Thus, claims 67-71, 73, 75, 83, 85 and 86 in present application and claims 1-13 in the patent are obvious variations of a pharmaceutical composition comprising a peg-EPO conjugate having the in vivo biological activity.

11. Claims 67-76 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/014,363. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 67-76 in the instant application disclose a liquid pharmaceutical composition comprising a pegylated EPO such as EPO linked to $-\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$ having the in vivo biological activity. This is an obvious variation in view of claims 1-16 in the copending application which disclose a conjugate comprising an EPO glycoprotein having N-terminal α -amino group and one poly(ethyleneglycol), where EPO is linked to $-\text{CO}-(\text{CH}_2)_x-(\text{OCH}_2\text{CH}_2)_m-\text{OR}$, and a pharmaceutical composition comprising the conjugate. Both the claims of the instant application and the claims of the copending application are directed to a pharmaceutical composition comprising a peg-EPO conjugate. Claims 67-76 in present application and claims 1-16 in the copending application are obvious variations of a pharmaceutical composition comprising a peg-EPO conjugate having the in vivo biological activity.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

In response, applicants cite the same reason as previously indicated (see pages 15-16 of the response). The ground of rejection remains until all other issues resolved.

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12. Claims 23-35, 38-42, 51-55, 59-61, 67-77 and 83-89 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-59 of copending Application No. 10/780,297 (US 2004/0147431). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 23-35, 38-42, 51-55, 59-61, 67-77 and 83-89 in the instant application disclose a liquid pharmaceutical composition comprising a pegylated EPO having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and a liquid pharmaceutical composition comprises a therapeutically effective amount of EPO product and a solution of a specific multiple charged inorganic anion and buffer at pH 6 to 6.5. This is an obvious variation in view of claims 1-59 in the copending application which disclose a liquid pharmaceutical composition consisting essentially of an EPO glycoprotein product having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and the liquid composition comprises a therapeutically effective amount of EPO product and a solution of a specific multiple charged inorganic anion and buffer at pH 6 to 6.5. Both the claims of the instant application and the claims of the copending application are directed to a pharmaceutical composition comprising an EPO glycoprotein product, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0. Claims 23-35, 38-42, 51-55, 59-61, 67-77 and 83-89 in present application and claims 1-59 in the copending application are obvious variations of a pharmaceutical composition comprising an EPO glycoprotein product having the in vivo biological activity, a multiple charged inorganic anion and a buffer at pH of 5.5 to 7.0, and the liquid composition comprises a therapeutically effective amount of EPO product.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 35, 61, 83, 84, 88 and 89 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 35 is indefinite because claim 35 has the same scope as claim 34. The limitation "10 to 50 mmole per liter of said solution" in claim 35 is already cited in the independent claim 26.

14. Claim 61 recites the limitation "40 mM arginine" in lines 1-2. There is insufficient antecedent basis for this limitation in claims 59 and 26.

15. Claims 83, 84, 88 and 89 are indefinite as to a composition containing an EPO product, arginine and sodium sulfate with a pH 6 to 6.5 or pH 6.2, since arginine has a pKa of 1.8, 9 and 12.5, and H₂SO₄ is a strong acid, it is not clear how the composition can have a pH about 6-6.5 without a buffer reagent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

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has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

16. Claims 23-25 are rejected under 35 U.S.C. 102(e) as anticipated by Burg *et al.* (U. S. Patent 6,340,742, filed June 28, 2000).

Burg *et al.* disclose a conjugate of erythropoietin (EPO) having at least one free amino group and having in vivo biological activity with poly(ethylene glycol) (PEG), wherein the conjugate comprises an EPO glycoprotein such as EPO (SEQ ID NO:1 or 2; column 3, lines 8-27) and analogs thereof which have human EPO modified by the addition of 1-6 glycosylation sites and the glycoprotein is covalently linked to 1-3 lower-alkoxy poly(ethylene glycol) groups via a linker of the formula $-C(O)-X-S-Y-$, where X is $-(CH_2)_k-$ or $-CH_2(O-CH_2-CH_2)_k-$, k is 1-10; Y is the structure shown at column 2, lines 15-35; and the average molecular weight of each PEG moiety is about 20 to 40 kDa and the molecular weight of the conjugate is 51 to 175 kDa (column 1, line 64-column 2, line 40); and a composition comprising the conjugate and BSA-PBS for administering to healthy mice (Example 4; claims 23-25).

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Conclusion

17. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Patent Examiner



**CHIH-MIN KAM
PATENT EXAMINER**

CMK
March 10, 2005